UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/530,363	05/01/2000	JEAN GABERT	1721-21	5387

7590 01/02/2003

NIXON & VANDERHYE
1100 NORTH GLEBE ROAD
8TH FLOOR
ARLINGTON, VA 22201-4714

EXAMINER
SPIEGLER, ALEXANDER H

ART UNIT	PAPER NUMBER
1637	19

DATE MAILED: 01/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/530,363	GABERT, JEAN	
	Examiner	Art Unit	
	Alexander H. Spiegler	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *September 25, 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 25th, 2002 has been entered.

2. Currently, claims 17-39 are pending. This action is made NON-FINAL. Any objections and rejections not reiterated below are hereby withdrawn.

Specification

3. The disclosure is objected to because of the following informalities:

A) In claim 39, the claim recites, "An *in vitro* diagnostic method...*in vitro*, comprising". The use of *in vitro* at the end of the preamble appears to be superfluous, and could be deleted from the claim.

B) Claim 39, recites "identifying the DNA sequences involved. --". The " --" should be deleted, since it appears to be a typographical error.

C) Claim 32 is objected to because a kit claim cannot depend from a method, wherein the method does not recite said kit.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 17-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 17-39 are indefinite over "sequences involved in pathologies associated with rearrangements" because it is not clear as to what "pathologies" are. The term "pathology" as defined by the National Center for Biotechnology Information is "A specialty concerned with the nature and cause of disease as expressed by changes in cellular or tissue structure and function caused by the disease process." (see MeSH Browser reference). Therefore, it would not be clear as to what "pathologies associated with rearrangements" are, considering that pathology is the study of the nature and cause of disease.

B) Claims 17-39 are indefinite over "one of the primers being complementary to the nucleotide sequence of the target gene" because "the nucleotide sequence" lacks antecedent basis.

C) Claims 17-39 are indefinite over "a complementary anchored primer" because is it not clear what a "complementary anchored primer" is, and it is not defined in the specification. What is the anchored primer complementary to?

D) Claims 17-39 are indefinite over "all the DNA sequences adjacent to the target gene are amplified" because it is not clear what constitutes "all the DNA sequences adjacent to the target gene". What sequence is considered to be "adjacent to the target gene".

E) Claims 17-39 are indefinite over "or any adjacent DNA sequences" because it is not clear as to what "adjacent sequences" are being referred to. Does this refer to adjacent sequences to the target gene?

F) Claim 21 over "and 10 to 20 T nucleotides" because it is not clear whether the 40 to 60 nucleotides must have at least 10 to 20 T nucleotides, or the primer consists of a cassette of 40 to 60 nucleotides, and additionally 10 to 20 T nucleotides. If Applicants mean the latter, do these 10 to 20 T nucleotides have to be adjacent to each other (as in an oligo-T primer) or can these additionally 10 to 20 T nucleotides be dispersed amongst an additional sequence of an unspecified length.

G) Claim 23 over "genome DNA or RNA" because it is not clear as what "**genome** DNA or RNA" means. It is not clear if applicants are referring to "genom**ic** DNA". Also it is not clear whether claim 23 is a second PCR reaction (i.e. nested PCR) reaction (since it is not clear as to what PCR is being referred to in step b).

H) Claim 23 over "the fusion of which is to be detected" because it is not clear as to what is being fused.

I) Claim 23 over "the PCR products" because it is not clear whether this refers to products obtained in step b of claim 23 (although, the actual recitation of "obtaining PCR products" is not present) or in step b of claim 39.

J) Claim 23 because it is not clear as to how a positive detection on the upstream probe and a negative detection on the downstream probe "correspond[s] to a rearrangement of the target genes". In other words, it is not clear as to whether a positive detection on the upstream probe and a negative detection on the downstream probe are the only conditions where rearrangements are found. (i.e. what corresponds to rearrangements of the target genes). It is also noted the claim is original only drawn to a target gene, not target genes. Furthermore, it is not clear as to what is meant by "the known partner genes corresponding to the absence of fusion

with a known fusion partner". First, what are "the known partner genes"? This recitation lacks antecedent basis. Also, it is not clear as to what genes constitute "genes corresponding to the absence of fusion with a known fusion partner". The specification is silent on definition of this recitation.

K) Claim 25 over "with a cassette" because it is not clear what "cassette" is being referred to. Also, "the oligonucleotide cassette" lacks antecedent basis.

L) Claim 26 because "the first MLL primer", "the oligonucleotide cassette", and the RT step lack antecedent basis. Additionally, it is not clear when the first nested amplification cycle occurred, thus, it is not clear that this is the second nested amplification cycle.

M) Claim 27 is indefinite because is it not clear that the PCR products are those obtained in step b of claim 39, and if they are not, it is not clear as to how this claims should depend from claim 24. In addition, "the hybridization products", "the enzyme substrate", "the probe/PCR product reactive mixture" and "the product" lack antecedent basis.

N) Claim 28 over "ribozymes MLL gene-specific" because it is not clear as to what it meant by this recitation, and furthermore, it is not defined in the specification.

O) Claim 28 over "the PCR products" because it is not clear whether this is referring to the PCR products in step b of claim 39. Also, "the so-obtained PCR products" lacks antecedent basis. Finally, Claim 28 is indefinite over "probes complementary to known partners" because it is not clear as to what constitutes or what is meant by "known partners".

P) Claims 32-38 are indefinite because it is not clear as to what are the necessary components of the claimed kit, since it is not clear what the target gene is (and therefore it is not

clear what the primers (or probes) specific for said target gene could be). Additionally, it is not clear as to reagents are necessary for carrying out anchored PCR and detection.

Q) Claim 33 over "the gene of the polypeptidic nucleic acids or of the ribozymes" because this recitation lacks antecedent basis, and it is not clear what is meant by this recitation. Also, it is not clear what agent is capable of cleaving or blocking "the gene of the polypeptidic nucleic acids or of the ribozymes".

R) Claim 36 because it is not clear as to how both the probes and streptavidin are coupled to plates.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 17-26 and 28-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Corral et al. (PNAS (1993) 90: 8538-42).

Corral teaches the detection of rearrangements with the MLL gene associated with various leukemias (see abstract), wherein a patient is subjected to an anchored PCR, comprising:

a) amplifying DNA or cDNA by one or more PCR, with one pair of primers with one pair of primers, one of the primers being complementary to the nucleotide sequence of the target gene, the other primer being a complementary anchored primer, wherein all the DNA sequences adjacent to the target gene are amplified (pg. 8539),

b) obtaining PCR products (pg. 8539),

c) hybridizing the PCR products with probes specific for either the target gene or any adjacent DNA sequences (pgs. 8539-8541)

d) detecting the presence of rearrangements of the target gene, and, if any rearrangement is detected, identifying the DNA sequences involved (pgs. 8539-8542).

Corral teaches that primers consisted of 25-40 nucleotides (pg. 8539), the use of labeled nucleotide probes (pgs. 8538-8540), subjecting a patient's genome DNA or RNA by a restriction enzyme (pg. 8538), and various probes for detection, such as upstream and downstream probes (pg. 8541). Additionally, the reference teaches the MLL gene undergoes chromosomal translocation in acute leukemia resulting in gene fusion with AF4 and ENL (see abstract). Furthermore, the reference teaches that the breakpoints of these translocations create this fusion of the MLL gene and the AF4 gene (pg. 8538). The reference also teaches the use of a primer EX5NP (MLL exon 5 specific primer) in a reverse-anchored-PCR reaction (pg. 8539).

8. Claims 32-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Cerelli et al. (USPN 5,620,861).

Cerelli teaches:

"In an alternative embodiment of a kit having a solid-phase support, the binding agent (binding molecule) attached to the support is the antibody reagent described in Section II. The antibody may be attached to the solid support by a variety of known methods, including chemical derivatization or high-affinity binding of the antibody by support-bound protein A or anti-IgG antibody, for example, according to standard methods. In this embodiment, the kit may additionally include a pyridinoline reagent which is effective to compete with N-Pyd in a sample for binding to the antibody reagent on the support. For detection purposes, the pyridinoline reagent may include a reporter-label attached covalently to pyridinoline (i.e., the reagent can be a reporter-labeled pyridinoline). Alternatively, the pyridinoline reagent may be reporter-labelable, in that the pyridinoline reagent can include Pyd conjugated to an agent such as biotin or streptavidin, for example, for recognition by a corresponding reporter-labeled streptavidin or biotin molecule." (col. 13).

9. Claims 32-35 and 37-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Chee et al. (USPN 5,837,832).

Chee teaches:

"DNA chips containing arrays of oligonucleotide probes can be used to determine whether a target nucleic acid has a nucleotide sequence identical to or different from a specific reference sequence. The array of probes comprises probes exactly complementary to the reference sequence, as well as probes that differ by one or more bases from the exactly complementary probes." (see abstract).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Corral et al. (PNAS (1993) 90: 8538-42), as applied to claims 17-26 and 28-30 above, in view of Hoeltke et al. (Cellular and Molecular Biology (1995) 41(7): 883-905).

The teachings of Corral are presented above. Specifically, Corral teaches the detection of rearrangements with the MLL gene associated with various leukemias. However, Corral does not teach the method of detection using a digoxigenine system.

Hoeltke teaches an overview of the digoxigenine system and teaches that it is advantageous over previous detection methods, such as the biotin/streptavidin system, since the digoxigenine system is more specific and sensitive (see whole document, especially, column 1 on page 884).

In view of the teachings of Hoeltke, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Corral so as to have detected fusion transcripts using the digoxigenine system, in order to have achieved the benefit of providing a more specific and sensitive means of detection.

Conclusion

12. No Claims are allowable.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (703) 305-0806. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014. Applicant is also invited to contact the TC 1600 Customer Service Hotline at (703) 308-0198.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Alexander H. Spiegler
December 30, 2002

GARY BENZION, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600